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Original Research Article

Study of drug utilization in cardiovascular emergency at a rural teaching hospital in Tamilnadu, India

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ABSTRACT

Background: Cardiovascular disease is a common term which encompasses a range of disorders that affect the heart. Cardiovascular disease is the leading cause of death among men and women in India and across the globe. There is evidence of irrational drug use in cardiovascular disorders. Drug utilization study is used to evaluate the rationality of medication use. The objective of this study was to observe the most frequently treated emergency cardiovascular diseases and to study the prescribing pattern among inpatients admitted in CICU Unit of tertiary care teaching hospital.

Methods: A retrospective, observational drug utilization study was designed to evaluate the drug prescribing pattern in cardiovascular emergency patients admitted in CICU unit of tertiary care teaching hospital. Study was carried out for a duration of 4 months. Data were collected from patient case reports after getting permission from Medical superintendent of hospital. Prescribing pattern of drugs were studied based on WHO indicators.

Results: Total 150 patients were included in the study. Most common cardiovascular emergency reported was Myocardial infarction (60.66%) followed by Angina pectoris (24.66%). The most common comorbidities found along with cardiovascular emergency were hypertension (62.66%) followed by Diabetes mellitus (15.33%). Most prescribed cardiovascular drugs were from the category of hypolipidemics (94.66%) and anti-platelets (92.66%). Average number of drugs per prescription was found to be 9.42. Average hospital stay per patient was found to be 4.25 days. Percentage of drugs prescribed by generic name was 70.66%. Percentage of drugs prescribed from essential drug list and National list of essential medicines were 87.4% and 97.23% respectively.

Conclusions: All the drugs prescribed were according to the current guidelines. Majority of the drugs were prescribed in generic form.

Keywords: Cardiovascular emergency, Drug utilization study, Generic drugs, Prescription auditing

INTRODUCTION

Cardiovascular diseases (CVDs) end the lives of 17.9 million individuals consistently, 31% of all worldwide deaths; setting off these diseases which show basically as heart attacks and strokes include tobacco use, unfortunate eating regimen, physical inactivity and the hurtful

utilization of liquor; these thus appear in individuals as raised blood pressure, hoisted blood glucose, overweight and obesity, risks detrimental to cardiac wellbeing.¹

The Indian subcontinent also experiences a huge loss of productive working years due to CVD demise.

Drug utilization study is used to evaluate the rationality of medication usage. It gives a positive input to prescribing physicians and help them to alter treatment strategies whenever necessary, identify, and right the weaknesses assuming any, hence giving the patients a rational and cost-effective treatment. Attributable to defencelessness of patient with CVDs to different complications, drug interactions and adverse events, these study tools are must in every hospital.

Prescription pattern is necessary, as it plays an important role in conveying message from prescriber to a patient. The use of least number of drugs to obtain best possible effect in the shortest period and that too at reasonable cost will be highly appreciable to achieve so called rationality in prescription.² Inappropriate use of medicines, development of resistance and economic burden on patients and the society are the consequences of irrationality.

The objective of this study was to observe the most frequently treated emergency cardiovascular diseases and to study the prescribing prevalence among inpatients admitted in CICU Unit of the hospital, using WHO drug indicators.

METHODS

It was a retrospective observational study to evaluate the drug prescribing pattern in cardiovascular emergency patients admitted to CICU of a tertiary care teaching hospital of south India. Study was carried out for a duration of 4 months (September 2018- December 2018).

Inclusion criteria

Data of patients diagnosed with CVDs and admitted to the CICU were included in the study.

Exclusion criteria

Incomplete case records and patients referred or discharged from hospital <24 hrs were excluded.

Study procedure

Using the 150 medical records data's like demographic details (age and sex), cardiovascular emergency, diagnosis and prescription details, average duration of stay in the hospital, outcome of the patient, number of drugs/prescriptions, percentage of drugs prescribed by generic name and percentage of drugs which are included in the essential drug list were collected. Data were collected by PharmD interns. Data were recorded as per WHO guidelines.

Statistical analysis

Data were analysed as per WHO guidelines given in WHO manual "How to investigate drug use in health facilities".

The information extracted was entered in Microsoft Excel sheet. Demographic data were analysed in the form of percentage and average.

RESULTS

Authors have analysed data of 150 patients. Out of 150 patients, 93 (62%) were males and 57 (38%) were females (Figure 1), which indicates that cardiovascular emergency was more in male when compared to female. Myocardial infraction and Angina pectoris are the two groups of Ischemic heart disease.³ Table 1 indicates that common cardiovascular emergency was MI (60.66%), Angina pectoris (24.66%) followed by CCF (13.33%) and Arrhythmia (1.33%). Gender wise distribution based on diseases is shown in Table 2.



Figure 1: Gender wise distribution of cardiovascular emergencies in this study.

Table 1: Most common cardiovascular emergenciesreported in this study.

Cardiovascular emergencies	No. of patients	Percentage
MI	91	60.66%
Angina pectoris	37	24.66%
Arrhythmias	2	1.33%
CCF	20	13.33%
Total	150	100%

MI: Myocardial Infarction, CCF: Congestive Cardiac Failure

Table 2: Gender wise distribution based on diseases.

Cardiovascular	Tatal	Gender		
emergencies	Total	Male	Female	
MI	91	56 (37.33%)	35 (23.33%)	
Angina pectoris	37	23 (15.33%)	14 (9.33%)	
Arrhythmias	2	2 (1.33%)	0	
CCF	20	12 (8%)	8 (5.33)	
Total	150	93 (62%)	57 (38%)	

MI: Myocardial Infarction, CCF: Congestive Cardiac Failure



Figure 2: Age-wise distribution of male and female patients.

 Table 3: Association of other comorbidities with the cardiovascular emergencies reported in our study.

Comorbidities	No. of patients	Percentage
HTN	94	62.66
Dyslipidemia	5	3.33
DM	23	15.33
CVA	2	1.33
Gastritis	1	0.66
Hypothyroidism	4	2.66
Anemia	3	2.0
COPD	1	0.66
Acute pulmonary edema	2	1.33
CKD	5	3.33
Asthma	3	2.0
Seizures	4	2.66
ТВ	2	1.33
Fibroid uterus	1	0.66

HTN: Hypertension, DM: Diabetes Mellitus, CVA: Cerebrovascular accident, COPD: Chronic Obstructive Pulmonary Disease, CKD: Chronic Kidney Disease, TB: Tuberculosis

Figure 2 shows the age wise distribution of male and female patients, in which incidence of cardiovascular emergency was found to be more in the age group of 51-70 years in both the genders and was significantly low in age group of 31-50 years.

Table 3 shows the association of other comorbidities with the cardiovascular emergencies in our study, Hypertension and diabetes mellitus were the most commonly found comorbidity.

Hypolipidaemic 142 (94.66%) and antiplatelets 139 (92.66%) were the most common classes of cardiovascular drugs prescribed followed by anticoagulants 80(53.33%) as shown in Table 4 and 5.

Out of 91 patients diagnosed with MI 50 patients had STEMI. Streptokinase and reteplase were the fibrinolytics

used. Intravenous furosemide was the most commonly used diuretic followed by spirinolactone. Inotropes like Dopamine, dobutamine and noradrenaline were used more commonly (Table 5).

Table 4: Various classes of cardiovascular drugs prescribed.

Drug class	No. of prescriptions	Percentage
Beta Blocker	36	24
ACE Inhibitors	27	18
ARB's	14	9.33
Diuretics	59	39.33
Anti-platelet	139	92.66
Anti-coagulant	80	53.33
Fibrinolytics	27	18
Hypolipidemic	142	94.66
Calcium		
channel	21	14
blockers		
Anti-anginals	26	17.33
Cardiac	7	4.66
glycosides	-	
Anti-arrhythmia	2	1.33
Inotropes	15	10
Vasodilator	2	1.33

ACE: Angiotensin Converting Enzyme, ARB: Angiotensin Receptor blocker

Improvement was seen in 123 (82%), while discharge at medical request was seen in 24 (16%) as shown in Table 6.

Table 7 shows the ATC/DDD classification and utilization rate of drugs. DDDs mentioned here in the table is obtained from WHO ATC/DDD website. This study shows that; Atorvastatin, ivabradine, ramipril, enalapril, furosemide is over utilised, since the PDD/DDD ratio is greater than 1.

Comparably Metoprolol, carvedilol, Telmisartan, spironolactone, warfarin, Amlodipine, cilnidipine, isosorbide di nitrate, ranolazine, dobutamine, noradrenaline is all under-utilised since PDD/DDD ratio being less than 1. Drugs which showed PDD/DDD ratio equal to 1 complying with the WHO ATC/DDD index include streptokinase, rosuvastatin, aspirin, clopidogrel and digoxin.

Table 8 depicts the analysis of prescription pattern according to drug use indicators. 70.66% of drugs were prescribed in generic name, 29.33% were prescribed by brand name, 30.46% prescriptions were seen to contain injections, Average number of drugs per prescription was seen to be 9.42. 18.66% of prescription contained antibiotics. Average duration of hospital stay per patient was studied as 4.25 days. 87.4% of drugs prescribed were from Essential Drug list (EDL) 2016-2018. 97.23% of drugs prescribed were from national list of essential medicines (NLEM) 2015.

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Drug class	Drug name (generic name)	Number of prescriptions	Percentage of prescription (%)
Beta-blocker	Atenolol	1	2.77
	Metoprolol	29	80.55
	Carvedilol	4	11.11
	Bisoprolol	2	5.55
ACE Inhibiter	Ramipril	4	16.66
ACE Inhibitors	Enalapril	23	85.15
	Losartan	3	21.42
AKB	Telmisartan	11	78.57
	Furosemide	48	81.35
Dimetica	Spironolactone	7	11.86
Diuretics	Metolazone	1	1.69
	Hydrochlorothiazide	3	5.08
	Aspirin	32	23.02
A (* 1 / 1 /	Clopidogrel	7	5.03
Anti-platelet	Clopidogrel A	98	70.50
	Ticagrelor	2	1.43
Anti-coagulant	Enoxaparin	48	60
	Warfarin	25	31.25
	Acenocoumarol	4	5
	Fondaparinux	3	3.75
Elle al a clastica	Streptokinase	25	92.5
Fibrinolytics	Reteplase	2	7.40
II	Atorvastatin	138	97.18
Hypolipidemics	Rosuvastatin	4	2.8
Calcium channel	Amlodipine	19	90.47
blocker	Cilnidipine	2	9.52
	Nitroglycerin	15	57.69
Anti-anginals	Ivabradine	4	15.38
	Isosorbide di nitrate	3	11.53
	Ranolazine	1	3.84
	Trimetazidine	1	3.84
	Nicorandril	2	7.69
Cardiac glycosides	Digoxin	7	100
Anti-arrhythmics	Amiodarone	2	100
	Dopamine	4	26.66
Inotropes	Dobutamine	6	40
	Noradrenaline	5	33.33
Vasodilator	Hydralazine	2	100

ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker

Table 6: Outcome of Cardiovascular emergency patients treated in this study.

Cardianagoular amongon sing	Total	Outcome		
Cardiovascular emergencies		Discharge	Death	DAMA
MI	91	85	1	5
Angina pectoris	37	25	0	12
Arrhythmias	2	2	0	0
CCF	20	11	2	7
Total	150	123 (82%)	3 (2%)	24 (16%)

MI: - Myocardial infarction, CCF: - Congestive cardiac failure

DISCUSSION

Drug utilization study is utmost important in different health care setups to analyse the behaviour of use of medicines by the society and to impart safe health care. Inappropriate use of medicines, development of resistance and economic burden on patients and the society are the consequences of irrationality.

Drug	ATC code	PDD	DDD	PDD/DDD
Atorvastatin	C10AA05	25.70mg	20mg	1.285
Rosuvastatin	C10AA07	70mg	10mg	7
Amlodipine	C08CA01	3.42mg	5mg	0.684
Cilnidipine	C08CA14	5mg	10mg	0.5
Isosorbide di nitrate	C01DA08	10mg (sublingual)	20mg (sublingual)	0.5
Ranolazine	C01EB18	1g	1.5g	0.666
Ivabradine	C01EB17	15mg	10mg	1.5
Aspirin	B01AC06	1 tablet	1 tablet	1
Clopidogrel	B01AC04	75mg	75mg	1
Digoxin	C01AA05	0.25mg	0.25mg	1
Amiodarone	C01BD01	0.2g	0.2g	1
Dobutamine	C01CA07	0.25g	0.5g	0.5
Noradrenaline	C01CA03	4mg	бmg	0.666
Metoprolol	C07AB02	0.05g	0.15g	0.333
Carvediol	C07AG02	25mg	37.5mg	0.666
Ramipril	C09AA05	5mg	2.5mg	2
Enalapril	C09AA02	17.82mg	10mg	1.782
Telmisartan	C09CA07	36.36mg	40mg	0.909
Furosemide	C03CA01	46.66mg	40mg	1.166
Spironolactone	C03DA01	50mg	75mg	0.666
Warfarin	B01AA03	3mg	7.5mg	0.4
Streptokinase	B01AD01	1.5 million units	1.5million units	1

Table 7: PDD/DDD ratio of cardiovascular emergency drugs used.

ATC Code: Anatomical Therapeutic Chemical Classification Code, DDD: - Daily defined dose, PDD: Prescribed daily dose.

Table 8: WHO drug prescribing indicators.

Drug use indicators	Results			
% of drugs prescribed by brand name	29.33%			
% of drugs prescribed by generic name	70.66%			
% of prescriptions with an injection	30.46%			
% of prescriptions with antibiotics	18.66%			
Average No. of drugs per prescription	9.42			
Average hospital stay per patient	4.25 days			
Number of drugs prescribed fromNational List of Essential Medicines97.23%(NLEM)- 201597.23%				
Number of drugs prescribed from Essential Drug List (EDL)- 2016-2018	87.40%			

In the present study, out of 93 (62%) male and 57 (38%) female case sheets analysed; the incidence of cardiovascular emergency was most commonly found in the age group of 51-70 years in both the sexes suggesting that the elders are more prone to the cardiac events, which were in accordance with Kerkar SS et al.⁴ Here authors also found that incidence of cardiovascular diseases is higher in males than in females. After menopause oestrogen's protective effect on cardiac health declines, which could be a reason for increased incidence of cardiovascular disease in female patients, since in our study data shows females with age group 51-70 are affected the most.

Out of 91 MI cases, 56 (61.53%) were male and 35 (38.46%) were female. Most common comorbid conditions found in patients were hypertension 94 (62.66%) and diabetes mellitus 23 (15.33%), this observation was similar to those of H. Nagabhushan et al, and Pendhari SR et al.^{5,6} Most common cardiovascular emergency was found to be MI 91 (60.66%) followed by Angina pectoris 37 (24.66%), which were in agreement with the study conducted by Vakade KP et al.⁷

Hypolipidemics 142 (94.66%) and antiplatelets 139 (92.66%) followed by anticoagulants 80 (53.33%) were the most commonly prescribed drug classes. These results are in accordance with Kerkar SS et al, and Nagabhushan H et al.^{4,5} Apart from these; drug utilization rate of diuretics, beta blockers, ACE inhibitors were also seemed to be high.

Aspirin+Clopidogrel combination was the most common fixed dose combination antiplatelet drug present in prescriptions, this result is in agreement with the study done by Nooreen M et al.⁸ This dual combination therapy is recommended by ACC/AHA for the management of CAD. Atorvastatin was the commonest prescribed hypolipidemic agent, according to ACC/AHA guidelines and Atherosclerotic cardiovascular disease (ASCVD) Risk calculator, moderate to high intensity statin therapy should be used in persons aged 40 to 75 years without clinical ASCVD or diabetes but with an estimated 10-year ASCVD risk of 7.5% or greater, on the other hand if the 10-year risk of ASCVD is less than 7.5%, moderate intensity statin is equitable.⁹

Among ACE inhibitors, enalapril was the most use drug, furosemide was the most used diuretic agent, enoxaparin and warfarin were the agents among anticoagulants. Streptokinase was the most used fibrinolytic in our study centre. Amlodipine and nitroglycerin were the most used calcium channel blocker and anti-anginal respectively.

Dopamine was found to be the most used positive inotrope from our study followed by dobutamine and noradrenaline. This result is in accordance to the study done by Nagabushan H et al, and is contrast to the study conducted by Lavanya S et al, where adrenaline is the most frequently used positive inotrope followed by noradrenaline and dobutamine.^{5,10} This shows that there is a mark difference in the use of inotropes in patients with cardiovascular emergency.

Among non-cardiovascular drugs like Proton pump inhibitors, stool softeners, antiemetics, antacids and benzodiazepines were most commonly prescribed in our study.

Study conducted by Vakade KP et al, average stay in hospital was found to be 5.75 days, our study shows 4.25 as the average hospital stay. 70.66% of drugs were prescribed in generic form, 29.33% were prescribed in brand name, these results differ strikingly from the study conducted by Chandana N et al.¹¹ This also reflects that free medicines offered in the government hospital located in rural areas are generic drugs, which is highly appreciable. Number of prescriptions with an injection were 30.46% which is in conformity with study conducted by Aswani R et al, (34.99%) and much lower than the study by Kerkar SS et al.^{12,4} Advantage of parenteral drugs is their ability to enhance drug adherence, the data recorded above is important since parental medications add to the expense of the prescription, also majority of adverse effects occurs through this route of administration.

Motivation behind ATC/DDD framework is to fill in as an instrument for drug utilization studies and research so as to improve nature of drug using ACT/DDD system, categorises the drugs based upon their pharmacological and therapeutic properties. The DDD for each drug were taken from the WHO collaboration centre for drug statistics methodology ATC/DDD website.¹³ This concept applies that each individual who is endorsed a specific drug is taking the drug according to its respective DDD, overlooking the adjustment of the dosage for every illness and the patient related components. Prescribed daily dose (PDD) is defined as the average dose prescribed according to a representative sample of prescription. PDD will give the average daily amount of a drug that is actually prescribed.

Ratio of PDD and DDD is used to evaluate drug utilization data. If the ratio is less than 1, it may indicate underutilisation of drug and if ratio is greater than 1, then over utilization of the drug is inferred. This study shows Atorvastatin, ivabradine, ramipril, enalapril, that: furosemide is over utilised, since the PDD/DDD ratio is greater than 1. Comparably Metoprolol, carvedilol, Telmisartan, spironolactone, warfarin, Amlodipine, cilnidipine, isosorbide di nitrate, ranolazine, dobutamine, noradrenaline is all under-utilised since PDD/DDD ratio being less than 1. Drugs which showed PDD/DDD ratio equal to 1 complying with the WHO ATC/DDD index include streptokinase, rosuvastatin, aspirin, clopidogrel and digoxin. Study conducted by Hannan A et al, also showed somewhat similar results.¹⁴ Lot of discrepancies between prescribed and defined daily doses are seen. Nevertheless, it is imperative to take note of PDD that can fluctuate according to both the indicated diseases treated and national therapeutic practices. Also, the PDDs additionally change considerably between various nations, PDDs are regularly lower in Asian than in Caucasian populations. On account of this it might appear as though there is underutilisation or over utilization of specific drugs based on the requirement. ATC/DDD system by itself is not suitable for controlling choices about therapeutic substitution as it solely doesn't imply any judgement on efficacy or relative efficacy of drugs and group of drugs.15

Average number of drugs per prescription was found to be 9.42, which is akin to study conducted by Nagabhushan H et al, (7.8 ± 2.2) which shows polypharmacy, though they were prescribed for cardiovascular emergency.⁵ Polypharmacy is an area of concern for elderly patients since they are more prone to ADRs, thus cautious and insightful drug prescription strategy is by all accounts ready to dispose the vast majority of the cases of polypharmacy. 87.4% of drugs prescribed were from Essential Drug list (EDL) 2016-2018.¹⁶ 97.23% of drugs prescribed were from national list of essential medicines (NLEM) 2015 which is the reason why there was a very good positive outcome among therapy in patients during the treatment period.¹⁷

Sample size used in this study was very small (150) and also the duration of study was short (4 months). Results of this study cannot be extrapolated to general population since study was single centred (i.e. it was carried out in a single government hospital). If other regional hospitals had been included in the study better results would have been generated.

CONCLUSION

In this study authors found that drugs were prescribed rationally and accordance to current guidelines being practiced. Majority of the drugs were prescribed in generic form, therefore cost benefit for the patients. Polypharmacy could be supervised in elderly patients by following certain criteria's like Beers criteria and STOPP/START criteria, Unnecessary drug use by the patient should be identified by the health care team appointed and stopped. Moreover, tools like ARMOR (Assess, Review, Minimize, Optimize, Reassess) would be useful to evaluate polypharmacy in elderly patients.

Appointing competent clinical pharmacist at all tertiary care hospital setups could further add to the effectiveness in treatment and outcome both directly and indirectly.

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